

## **REMARKS**

### **I. Claim Amendments**

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 8, 10 – 12, and 14 - 17 are requested to be cancelled.

Claims 1 – 7, 9, 13, 18, 19, and 21 are currently being amended.

After amending the claims as set forth above, claims 1 – 7, 9, 13, and 18 - 21 are now pending in this application.

### **II. Restriction Requirement**

In response to the restriction requirement set forth in the Office Action mailed May 27, 2009, Applicants hereby provisionally elect Group I, claims 1 – 7, 9, 13, and 19 – 21, drawn to a nucleic acid probe, for examination, with traverse.

In response to the species requirement, Applicants hereby provisionally elect HLA-A, and sub-species HLA-A\_A, for initial search and examination, with traverse.

Applicants traverse the restriction requirement based on the particular distinctive features of the claims as amended. Applicants request withdrawal of the restriction requirement and search and examination of all pending claims.

This invention is directed to a method of HLA-A typing, i.e. to the determination of which polymorphic HLA-A alleles are expressed by a given subject. As explained in the specification (see page 2, lines 27-29), HLA-A typing is important for tissue transplantation, immunity and auto-immune diseases.

Many polymorphic HLA-A alleles are known in the prior art, and these polymorphic alleles are associated with several polymorphic SNPs (single nucleotide polymorphisms) at various positions of the HLA-A gene. From D5, it is clear that at least 98 polymorphic SNPs have been identified in the HLA-A gene.

However, the complete sequencing of the HLA-A gene or the analysis of all known polymorphic positions (at least 98) is not a convenient method for HLA-A typing, since it represents a time-consuming and costly method. More rapid and less expensive, but still reliable, methods are needed.

The method claimed in the present application comprises the determination of short DNA sequence elements (2-6 bases) at only 10 positions simultaneously: positions 98, 414, 539, 282, 571, 368, 256, 292, 238 and 270 (according to the numbering of the HLA-A gene starting at cDNA sequence position 1 of exon 1).

As indicated in the description, these 10 positions permit to provide a maximum number of subgroups which give best distinction between the frequent HLA-A alleles and the rest of the rare HLA-A alleles (see page 6 lines 5-11).

Each subgroup HLA-A\_A to O obtained by this method contain 2-30 HLA-A alleles (see Table I, page 10), which appear identical after performing the basic HLA-A typing method using the 10 selected positions.

In other words, if an HLA-A allele of a subject is found to belong to a particular HLA-A subgroup (A to O) using this basic HLA-A typing method, then this HLA-A allele is one the alleles belonging to said subgroup, as defined in Table I (see page 10).

The resolution of HLA-A typing can then be improved using two alternative methods:

• Claim 9:

An additional set of 9 positions (453, 527, 502, 81, 268, 559, 92, 123 and 396) are analyzed, resulting in a set of 19 positions (98, 414, 539, 282, 571, 368, 256, 292, 238, 270, 453, 527, 502, 81, 268, 559, 92, 123 and 396)

This results in a medium resolution of HLA-A typing (see page 8, lines 4-5), permitting to differentiate alleles that are frequent (A\*0101, A\*0201, A\*0301, A\*2301, A\*2402, A\*2902, A\*3001, and A\*3002) in the general population from ones that are rare (see page 5, lines 25-30).

• Claim 13:

Depending on the HLA-A subgroup (A to 0) obtained in the first step, a particular additional set of 1-25 positions is analyzed, which permits to resolve which allele of the subgroup is expressed by the subject.

This allows a higher HLA-A typing resolution since the allele is precisely determined.

In any case, the main advantage of the present invention is that for a given subject allele, only a reduced number of positions (10 in the basic method, 19 in the method of claim 9, and 11-36 in the method of claim 13) have to be analyzed to identify with a satisfying resolution the allele expressed by the subject.

This results in a simpler, quicker and less expensive, but still reliable, HLA-A typing method.

This method for HLA-A typing can be notably implemented using the set of primers described in Table IV.

Existence of a special technical feature

Cited document Pastinen et al does not disclose nor suggest that a simpler, quicker and less expensive, but still reliable, HLA-A typing method can be obtained by analysing a restricted set of 10 positions in HLA-A gene.

The method claims have been limited to the typing of HLA-A by analysis of a restricted set of 10 positions in HLA-A gene. Kit claim 18 has been limited to a particular pool of primers (those of Table IV), which have been specifically designed for the implementation of the method of claim 1, since Table IV consists of primers permitting to amplify the restricted set of 10 positions in HLA-A gene, as well as 9 additional positions permitting to achieve medium resolution (see claim 9).

The new and inventive special technical feature common to method and kit claims is thus the restricted set of 10 positions in HLA-A gene, as well as 9 additional positions of HLA-A gene permitting to improve typing resolution.

### **III. Conclusion**

Applicants believe that the present application is now in condition for search and examination of all pending claims. Favorable reconsideration of the restriction requirement for the claims as amended is respectfully requested.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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By 

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